UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,006	09/17/2001	Robert J. Schneider	5914-084-999	7849

20583 7590 03/09/2004

JONES DAY
222 EAST 41ST STREET
NEW YORK, NY 10017

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,006	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 22-30 are pending.

Response to Amendment

This is a response to the amendment, paper No. 10, filed 10/21/03. Claims 22-23 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not including this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-30 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous Office Action, because the specification, while being enabling for using an in vitro cell line system to demonstrate that the expression of recombinant hepatitis B virus (HBV) X protein (HBx) in cell line increase the activation of Src family tyrosine kinases, wherein the activation of the kinase, such as Pyk2, can be inhibited by calcium chelator EGTA or calcium channel poison or modulator cyclosporine A (CsA), does not reasonably provide enablement for having an in vivo method for treating patients infected with HBV by using any or all agents, which are able to modulate the cytosolic calcium concentration of a cells in vitro. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to made and use the invention commensurate in scope with these claims.

3. Applicants transverse the rejection and submit that the specification provides an in vitro assay for identification of genus compound that is able to reduce cytosolic calcium concentration will inhibit HBV replication. Because there is no animal system were universally accepted an animal models of HBV disease. Instead, cell-bases assays were used as more reliable predictions of efficacy of treating HBV infection.

4. Applicants' argument has been fully considered; however, it is not found persuasive because Office does not doubt the in vitro results presented in the specification, however, the in vitro results cannot be extrapolated into an in vivo practice. Moreover, there are several popular HBV animal models, such as Woodchuck hepatitis B model (Korba et al. Antimicrob Agents Chemother. 2000 Vol. 44, No. 6, pp. 1757-1760), murine model (Akbar et al. European Journal of Clinical Investigation 1999, Vol. 29, pp. 286-792) and duck model (Hantz et al. Antiviral Research 1999, Vol. 40, pp. 179-187) available in the art prior to the application was filed. Especially considering the broadly claimed scope of current application read on that any or all other calcium chelator capable of reducing the cytosolic calcium will be able to inhibit HBV replication and applicable for treating the patient infected with HBV in patients.

5. Furthermore, treatment of HBV patient with cyclosporine is always unpredictable. For example, Lau et al. (Transplantation 1989, Vol. 53, pp. 894-898, see abstract) reported treatment of HBV primary hepatocyte culture with cyclosporine increase the HBV replication (See Table 3 on page 283). Sandrini et al. (Nephrol Dial. Transplant. 1990, Vol. 5, pp. 525-530) also reported that treatment of HBV positive patients with cyclosporine increase the HBV DNA replication (See abstract). However, Nakanishi et al. also teach that treatment of a HBV positive patient with cyclosporine slightly reduce the HBV DNA replication (Internal Medicine 1998, Vol. 37, pp. 519-522, see abstract).

6. Therefore, the rejection is maintained unless Applicants provide more evidence that support the broadly claimed invention read on using any or all compounds that reduce the cytosolic calcium are able to treat HIB infection in patients.

New Ground of Rejections:

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 22-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakanishi et al. (Internal Medicine 1998, Vol. 37, No. 6, pp. 519-522).

3. Nakanishi et al. disclose a case report that a 57-year-old woman who is positive for the HBV received cyclosporine plus INF-α treatment. As result, the HBV-DNA levels was reduced. While Nakanishi et al. do not teach that the cyclosporine reduce the cytosolic calcium level or interferes with the activity of a mitochondrial calcium channel etc. the cyclosporine used by Nakanishi et al. has the same structure and biological function as that of claimed cyclosporine. Therefore, the claimed invention is anticipated by the cited prior art.

Conclusion

Claims 29-30 are free of prior art rejection. However, they are not in the condition for allowance because they dependent on the rejection claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
February 23, 2004

James C. Housel 3/8/04
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600